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537

Microparticles and exosomes differentially impact on endothelial cell function in coronary artery disease

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Background and Purpose: Microparticles (MPs) and exosomes are released by cells using different mechanisms. Thus, quantitative as well as qualitative changes of both particle populations, MPs and exosomes, in patients with coronary artery disease (CAD) might reflect an altered activation status of the endothelium, platelets and leukocytes. Moreover, they might exert differential effects on the target organs, such as the endothelium. Yet, alterations in both populations have not been studied side-by-side so far.

The aim of the study was to compare the impact of MPs and exosomes from healthy subjects and CAD patients on endothelial cell (EC) functional characteristics.

Methods: MPs and exosomes were isolated by stepwise filtration and ultracentrifugation from citrate-plasma and verified by electron microscopy and dynamic light scattering. MP and exosome fractions, as well as the vehicle (PBS), were added to human arterial ECs and EC apoptosis, number, size, capacity for in vitro-reendothelialisation after scratching, expression of adhesion molecules ICAM-1 and VCAM-1 were assessed. In parallel, platelet-, endothelial- and leukocyte-derived MPs were quantified. In a separate sub-study, the same parameters were assessed in plasma of CAD patients undergoing standard medical rehabilitation or an exercise-based cardiac rehabilitation programme.

Results: MPs of healthy, but not of CAD patients supported in vitro re-endothelialisation, while exosomes had no influence. Exercise, but not standard rehabilitation improved CAD MP capacity to support in vitro rehabilitation. This was negatively correlated to the number of leukocyte- and endothelial-derived MPs, but not total or platelet MPs. EC number was negatively affected by exposure to CAD MPs. ANCOVA analysis identified disease, but not the particle type as influencing factor. Instead, apoptotic cell death was influenced by particle type, but not by the disease, and was not altered in rehabilitation. Similarly, ICAM-1 and VCAM-1 expression were enhanced on ECs after incubation with exosomes, but not with MPs, with no effect of disease or rehabilitation.

Conclusion: MPs and exosomes differentially affect endothelial cell function and underlie differential modulation in disease and rehabilitation. Those findings might in the future help to optimize and monitor cardiovascular therapy.